



UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER OF PATENTS AND TRADEMARKS
Washington, D.C. 20231
www.uspto.gov

| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|-----------------|-------------|----------------------|---------------------|------------------|
| 08/908,469 | 08/06/1997 | MANUEL BACA | PI1093PI | 9546 |

9157 7590 07/09/2002

GENENTECH, INC.
1 DNA WAY
SOUTH SAN FRANCISCO, CA 94080

[REDACTED] EXAMINER

HELMS, LARRY RONALD

[REDACTED] ART UNIT

[REDACTED] PAPER NUMBER

1642

DATE MAILED: 07/09/2002

34

Please find below and/or attached an Office communication concerning this application or proceeding.

| | | |
|-----------------------------|-----------------|--------------|
| Offic Action Summary | Application No. | Applicant(s) |
| | 08/908,469 | BACA ET AL. |
| Examiner | Art Unit | |
| Larry R. Helms | 1642 | |

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) Responsive to communication(s) filed on 08 May 2002.

2a) This action is FINAL. 2b) This action is non-final.

3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4) Claim(s) 1-42 is/are pending in the application.

4a) Of the above claim(s) 1-33 and 39-42 is/are withdrawn from consideration.

5) Claim(s) _____ is/are allowed.

6) Claim(s) 34-38 is/are rejected.

7) Claim(s) _____ is/are objected to.

8) Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9) The specification is objected to by the Examiner.

10) The drawing(s) filed on _____ is/are: a) accepted or b) objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) The proposed drawing correction filed on _____ is: a) approved b) disapproved by the Examiner.
If approved, corrected drawings are required in reply to this Office action.

12) The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a) All b) Some * c) None of:
1. Certified copies of the priority documents have been received.
2. Certified copies of the priority documents have been received in Application No. _____.
3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
* See the attached detailed Office action for a list of the certified copies not received.

14) Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
a) The translation of the foreign language provisional application has been received.

15) Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

| | |
|--|--|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) Paper No(s). _____ . |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ . | 6) <input type="checkbox"/> Other: _____ . |

Art Unit: 1642

DETAILED ACTION

1. Claims 1-42 are pending.
2. Claims 1-33, 39-42 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected inventions. Election was made without traverse in Paper No. 7.
3. Claims 34-38 are under examination.
4. The text of those sections of Title 35 U.S.C. code not included in this office action can be found in a prior Office Action.
5. The following Office Action contains some NEW GROUNDS of rejection.
6. NOTE: The following papers have not been made part of the permanent records of the United States Patent and Trademark Office (Office) for this application (37 CFR 1.52(a)) because of damage from the United States Postal Service irradiation process:

Mailroom Stamp Date

5/23/02

Certificate of Mailing Date

5/8/02

The above-identified papers, however, were not so damaged as to preclude the USPTO from making a legible copy of such papers. Therefore, the Office has made a copy of these papers, substituted them for the originals in the file, and stamped that copy:

**COPY OF PAPERS
ORIGINALLY FILED**

If applicant wants to review the accuracy of the Office's copy of such papers, applicant may either inspect the application (37 CFR 1.14(d)) or may request a copy of the Office's records of such papers (*i.e.*, a copy of the copy made by the Office) from the Office of Public Records for the fee specified in 37 CFR 1.19(b)(4). Please do **not** call the Technology Center's Customer Service Center to inquiry about the completeness or accuracy of Office's copy of the above-identified papers, as the Technology Center's Customer Service Center will **not** be able to provide this service.

If applicant does not consider the Office's copy of such papers to be accurate, applicant must provide a copy of the above-identified papers (except for any U.S. or foreign patent documents submitted with the above-identified papers) with a statement that such copy is a complete and accurate copy of the originally submitted documents. If applicant provides such a copy of the above-identified papers and statement within **THREE MONTHS** of the mail date of this Office action, the Office will add the original mailroom date and use the copy provided by applicant as the permanent Office record of the above-identified papers in place of the copy made by the Office. Otherwise, the Office's copy will be used as the permanent Office record of the above-identified papers (*i.e.*, the Office will use the copy of the above-identified papers made by the Office for examination and all other purposes). This three-month period is not extendable.

Response to Arguments

7. The rejection of claims 34-38 under 35 U.S.C. 102(a) as being anticipated by Baca et al (The Journal of Biological Chemistry 272:10678-10684, 4/18/97, IDS #14) is maintained.

The response filed 5/23/02 has been carefully considered but is deemed not to be persuasive. The response states that the Baca et al reference describes the inventors' own work and thus should not be deemed as prior art and a declaration from Dr. Leonard Presta was submitted with the response. Applicant's arguments in conjunction with the Katz-type declaration under 37 C.F.R. § 1.132, filed 5/23/02 (Paper No. 33), has been fully considered but not found convincing.

The Katz declaration acknowledges that the Baca et al publication sets forth the invention substantially as claimed (see page 2, paragraph 4 of declaration). While the declaration provides a satisfactory showing why Shane J. O'Connor is not an inventor of the instant claims. However, there is an ambiguity as to the contribution of Henry Lowman and Yvonne Chen, who are not listed as authors of the Baca et al reference. Given that the Baca et al reference teaches the claimed invention, as acknowledged by applicant, it is incumbent on applicants to provide a satisfactory showing which would lead to a reasonable conclusion that applicants alone, including Henry Lowman and Yvonne Chen are the inventors of the claimed invention.

See In re Katz, 687 F.2d 450, 215 USPQ 14(CCPA 1982). See MPEP 715.05.

Art Unit: 1642

8. The rejection of claims 34-38 under 35 U.S.C. 103(a) as being unpatentable over Ferrara et al (WO 94/10202, published 5/11/94) and further in view of Adair et al (WO 91/09967, published 7/11/91, IDS#4) and Yelton et al (The Journal of Immunology 155:1994-2004, 1995) is maintained.

The response filed 5/23/02 has been carefully considered but is deemed not to be persuasive. The response states that by simply applying humanization methods of Adair et al or Yelton et al to the murine antibodies of Ferrara et al one of ordinary skill in the art would not have had a reasonable expectation of success to produce a humanized anti-VEGF antibody variant that minimized the HAMA immunogenicity as well as binds with strong affinity that is more than about 6 fold of the parent, inhibits VEGF-induced endothelial cell proliferation in vitro at 5nM and inhibits VEGF-induced angiogenesis in vivo. The response then argues that Adair et al teaches a general protocol for one skill in the art to try different arrangements of residues and one would have to pick and choose without sufficient guidance or expectation of success (see page 4 of response) and Adair et al showed that even those with increased binding affinity behaved differently in an unpredictable manner in biological activities. The response then addresses the Yelton et al reference by stating that CDRs were altered not frameworks and the binding affinity does not necessarily correlate with binding affinity to tumor cells (see page 5-6 of response).

In response to these arguments, while Adair et al does teach a general method, the method can be performed on any antibody and all that is required is the screening of

many altered antibodies which would not be undue and would have been routine at the time the claimed invention was made. In addition, while the response is directed to an example in Adair et al where binding to cells were reduce even thought the affinity was increased, there is examples in Adair et al, for example the OKT3 humanized antibody which has good binding to cells and had very similar binding in a competition assay (see pages 36 and 51). Thus, there are examples in Adair et al where high affinity and good in vivo binding is taught. In addition, in the example described in the response which showed a lowering in the ability of the antibody to compete with TNF, it would be obvious that a higher concentration would compete better and this is important in view that the claims require a concentration of 5mg/kg which is at a high dose. In response to the Yelton et al argument, first it is not clear what mutations in the CDR vs mutations in the framework have to do with the argument, because the claims are directed to a product not a method of making the product. In addition, Yelton et al does suggest altering the frameworks (see page 2001). Turning to the example in the response, there were several mutant antibodies made and while the M4 was not optimal, the M# antibody had improved affinity and better binding to H3396 cells (see page 1999 left column last paragraph). Thus, both Adair et al and Yelton et al teach that combining mutations can lead to the desired characteristics. This is important because Ferrera et al teach that the antibodies encompassed in Ferrera et al are those that are humanized and have characteristics of high binding affinity and inhibiting angiogenic activity of VEGF at least about 50% and teach the A673 tumor model (see page 8).

The following is a NEW GROUND of rejection

Claim Rejections - 35 USC § 102

9. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(f) he did not himself invent the subject matter sought to be patented.

10. Claims 34-38 are rejected under 35 U.S.C. 102(f) because the applicant did not invent the claimed subject matter.

Applicant's arguments in conjunction with the Katz-type declaration under 37 C.F.R. § 1.132, filed 5/23/02 (Paper No. 33), is noted.

The Katz declaration acknowledges that the Baca et al publication sets forth the invention substantially as disclosed (see page 2, paragraph 4 of declaration). While the declaration provides a satisfactory showing why Shane J. O'Connor is not an inventor of the instant claims. However, there is an ambiguity as to the contribution of Henry Lowman and Yvonne Chen, who are not listed as authors of the Baca et al reference. Given that the Baca et al reference discloses the claimed invention, as acknowledged by applicant, and teaches that recited in claim 34 part (a), it is incumbent on applicants to provide a satisfactory showing which would lead to a reasonable conclusion that applicants alone, including Henry Lowman and Yvonne Chen are the inventors of the claimed invention. It is unclear if parts (b) and (c) in claim 34 are an inherent property of the antibody which has the property of part (a) and if it is an inherent property of the antibody, what inventive contributions did Henrry Lowman and

Art Unit: 1642

Yvonne Chen contribute to the claimed invention. See In re Katz, 687 F.2d 450, 215 USPQ 14(CCPA 1982). See MPEP 715.05.

Conclusions

11. No Claims are allowed.
12. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

13. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Larry R. Helms, Ph.D, whose telephone number is (703) 306-5879. The examiner can normally be reached on Monday through Friday from 7:00

Art Unit: 1642

am to 4:30 pm, with alternate Fridays off. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anthony Caputa, can be reached on (703) 308-3995. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

14. Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center telephone number is (703) 308-4242.

Respectfully,

Larry R. Helms Ph.D.

703-306-5879

Sheela Huff
SHEELA HUFF
PRIMARY EXAMINER